

**ATTACHMENT A**  
**Remarks**

Claims 3-8 are pending in the present application. By this Amendment, Applicants have amended claims 3 and 5, and added new claims 7 and 8. Applicants respectfully submit that the present application is in condition for allowance based on the discussion which follows.

Claims 3-6 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nyamekye et al. (hereinafter "Nyamekye") in view of Narciso, Jr. (U.S. Patent No. 5,298,018) (hereinafter "Narciso"), Aizaw et al. (U.S. Patent No. 5,308,861) (hereinafter "Aizaw") and Antoshkiw et al. (U.S. Patent No. 4,471,779) (hereinafter "Antoshkiw").

Contrary to the obviousness-type rejection of claims 3-6, Applicants respectfully submit that the cited prior art, individually or in combination with one another, fails to teach or suggest all claim elements. Further, Applicants respectfully submit that there fails to be any reasonably apparent reason for one of ordinary skill in the art to modify the individual disclosures of the prior art to arrive at the claimed invention. Elements not taught or obvious in view of the prior art include: (1) a single administration of a photosensitizing compound, (2) a photodynamic treatment ("PDT") effected at a first and only time point of 0.5 to 6 hours after the single, sole administration of the photosensitizing compound necessary for PDT, using the claimed laser fluence of 1 to 10 J/cm<sup>2</sup>, and (3) total occlusion of a blood vessel using a completely inflated balloon catheter at the previously angioplasty-dilated and injured site in a blood vessel.

Contrary to the Examiner's assertion, Narciso, individually or in combination with the prior art, fails to teach or in any way make obvious a single administration of a

photosensitizing compound before or after an angioplasty treatment, as claimed.

Although the Examiner alleges that reciting a single treatment may include more than one treatment, such an interpretation is inconsistent with the clear claim language. For example, with regard to claim 3, although the transitional phrase, "said method comprising," may include additional steps not recited, the unambiguous meaning of the recited single time administration makes it clear that any additional process, in addition to those affirmatively recited, cannot contradict the recited single time administration. Therefore, having more than a single time administration would be contrary to the unambiguous claim language recited in claim 3.

With regard to claim 5, the transitional phrase, "said method consisting of," makes it even more unambiguous that the method is limited to just the recited steps. Although the Examiner alleges in the Response to Arguments section that the transitional phrase "consisting of" limits only the photosensitive compounds, such an interpretation is inconsistent with U.S. claim construction. M.P.E.P. § 2111.03 clearly states that the transitional phrase "consisting of" excludes any step not specified in the claim. Therefore, Applicants respectfully submit that the transitional phrase in claim 5, "consisting of," renders the claim limited to the steps recited and, therefore, claim 5 is limited to only a single administration of a photosensitive compound.

Moreover, Narciso clearly teaches that it is essential to have multiple administrations of a photosensitizer before, during or after angioplasty for a period of 5 to 18 days in order to block smooth muscle cell growth factor at all sites and to ensure that release of growth factor from platelets has terminated. Therefore, it would not have been obvious to one of ordinary skill in the art to modify the clear and unambiguous

teaching of Narciso, which necessarily teaches multiple administrations for a period of at least 5 to 18 days in order to arrive at the present method, which teaches a single administration. Accordingly, contrary to the Examiner's statement that an artisan would have been motivated to administer the compound once, depending on efficacy, Narciso teaches just the opposite, i.e. that multiple re-administrations are essential.

Based on the foregoing, Applicants respectfully submit that claims 3 and 5 are specifically directed to a single time administration of a photosensitizing compound to the exclusion of multiple administrations. Accordingly, Narciso, which teaches the necessity of multiple administrations, fails to anticipate the claimed single administration.

Furthermore, Applicants respectfully submit that contrary to the Examiner's assertion, Narciso does not teach the use of photodynamic therapy during a PTCA procedure. To the contrary, Narciso teaches that photodynamic therapy occurs anywhere from 5-18 days after a PTCA procedure. See, e.g., Narciso, column 2, lines 23-37, where Narciso teaches exposing the photosensitizer to light at a wavelength at which the photosensitizer absorbs light 5-18 days after the PTCA procedure. One of ordinary skill in the art would understand the term "photodynamic therapy" to mean a "process of activating a photosensitizer with light to cause cell necrosis" (Narciso, column 2, lines 40-42, emphasis added). The photosensitizer is "activated" by being irradiated with light at a wavelength which causes the photosensitizer to absorb light, causing cell lysis. Since the irradiation occurs 5-18 days after angioplasty (Narciso, column 2, lines 22-36), Narciso fails to teach or in any way

make obvious photodynamic therapy (irradiating a photosensitizer) during percutaneous transluminal coronary angioplasty (PTCA).

It should be stressed that administering a photosensitizer is not a photodynamic therapy. While administration of a photosensitizer is a prerequisite of photodynamic therapy, i.e. the irradiation of the photosensitizer, the administering of the photosensitizer itself is not photodynamic therapy. Furthermore, it must be noted that the photosensitizer initially administered during the angioplasty step or PTCA procedure is not the photosensitizer which is subject to photodynamic therapy, as repeated administration of the photosensitizer over 5-18 days is necessary to block the growth-factor binding sites on SMC cells, and the irradiation only occurs after a final administration of photosensitizer 5-18 days after the initial administration.

Moreover, the present method is distinguishable over the prior art by reciting a method which irradiates the single time administered photosensitizing compound from 0.5-6.0 hours after the single, i.e. sole, administration of a photosensitizing compound. The prior art fails to teach or in any way make obvious irradiating a photosensitizing compound within 0.5-6.0 hours of a single, and thus first, administration. To the contrary, Narciso clearly teaches multiple administrations for up to 5 to 18 days. Therefore, Narciso teaches that a minimum of at least 5 days must pass between the first administration of a photosensitizer and the irradiation. Accordingly, the prior art fails to teach or in any way make obvious irradiating 0.5-6.0 hours after a first and only administration. Since the prior art teaches irradiating more than 6 hours after a first administration of a photosensitizing agent, Narciso fails to teach or in any way make

obvious irradiating between 0.5-6.0 hours after that first administration and, in fact, teaches irradiating at least 5 days after a first administration.

Based on the foregoing, Applicants respectfully submit that the prior art fails to teach or in any way make obvious irradiating between 0.5 and 6.0 hours after a first and only, single administration of a photosensitizing compound.

In addition, the prior art fails to teach or in any way make obvious the present method of irradiating at a power or fluence of 1 to 10 J/cm<sup>2</sup> in the photodynamic therapy method claimed. To the contrary, the disclosed Narciso example, which provides the necessary parameters to practice its invention, uses SnET2 specifically as the photosensitizer and irradiates at about 660 nm at a light dose of 20 J/cm<sup>2</sup> (see, e.g., Narciso, column 8, last four lines), under conditions in which the bloodstream is allowed to flow in the form of a 0.25 nm thick annular bloodstream around the laser-irradiating optic fiber catheter between the catheter and the inner wall of the vascular vessel (Narciso, column 9, lines 17-33).

Although, in the Response to Arguments section, the Examiner alleges that it would have been obvious to optimize the dosage of Narciso to arrive at the claimed laser fluence, one of ordinary skill in the art would not have been led to modify the laser fluence to have the claimed wavelength and power without undue experimentation. The Narciso example uses a different photosensitizing agent, namely SnET2, compared with the claimed Npe6; Narciso discloses a laser wavelength of 660 nm, whereas the present invention uses a wavelength of 664 nm; and Narciso teaches bloodflow in the form of a 0.25 nm thick annular bloodstream when processing at the aforementioned parameters, whereas, in the present invention, the blood vessel is completely occluded

at the angioplasty site. There fails to be any metric or disclosure within the prior art which would lead one of ordinary skill to know how to modify the photosensitizer, laser wavelength, laser fluence and occlusion of the blood vessel to the extent claimed to arrive at the claimed parameters without undue experimentation. Moreover, there fails to be any reasonably apparent reason why one of ordinary skill in the art would have been led to make the necessary modifications in order to arrive at the claimed method.

Furthermore, the present method completely occludes the bloodstream between an inner wall of a vascular vessel at the site of a previous angioplasty treatment. The balloon catheter is completely inflated and an integrated optical fiber is used for irradiating the laser. Due to the numerous distinctions between the present method and that of Narciso, contrary to the Examiner's allegation, it would not have been a matter of routine experimentation by one of ordinary skill in the art to make such numerous modifications and arrive at the claimed processing parameters without undue experimentation. Moreover, the Examiner has failed to provide any evidence or allege any facts which would support such a conclusion that making the modifications alleged would not necessitate undue experimentation.

Moreover, one of ordinary skill in the art would fail to recognize that a decrease in laser fluence is possible, based on the method taught by Narciso. It is not until one considers the present method of total occlusion of blood, namely the total occlusion of blood using a balloon catheter within a vascular lumen at the site of a previous angioplasty treatment in order to conduct laser irradiation at that site using the claimed laser light wavelength, that one of ordinary skill in the art realizes that a decreased dose or fluence of 1 to 10 J/cm<sup>2</sup> is possible. Accordingly, it is completely unpredictable to

one of ordinary skill in the art, based on Narciso's teaching, to arrive at the claimed wavelength and fluence levels. Therefore, even if one were motivated to modify the disclosure of Narciso, it would take undue experimentation to arrive at the claimed parameters.

Further, the prior art fails to teach or in any way make obvious the total occlusion of a blood vessel via a completely inflated balloon catheter at a prior angioplasty site. Although the prior art may disclose inflation of a balloon catheter, the prior art fails to teach or in any way make obvious the complete interception of a bloodstream around an intervascularly inserted catheter during irradiation procedure. In the Response to Arguments section, the Examiner alleges that Applicants' argument "that Narciso fails to teach inflating a catheter balloon at the prior angioplasty-dilated site during PTD to exert an outward force of pressure on the blood vessel" is "not persuasive because this limitation is inherent to the PDT procedure . . . and . . . Narciso clearly disclose the use of photodynamic therapy during a PCTA procedure." However, contrary to the Examiner's allegation, Narciso fails to teach or in any way make obvious inflating a balloon catheter at the prior angioplasty site during photodynamic therapy, i.e. laser irradiation. Although Narciso discloses administering a photosensitizer before, during or after PCTA, nowhere does Narciso teach or in any way make obvious inflating a balloon catheter at the prior angioplasty site during the laser irradiation process, as claimed. Thus, although Narciso teaches a balloon inflation, possibly during an angioplasty step in advance of a subsequent irradiation process, nowhere does Narciso teach or in any way make obvious inflating a balloon catheter at the prior angioplasty site during the irradiation process. Accordingly, Narciso fails to teach or in any way make obvious the

claimed method, which recites inflating a balloon catheter at a prior angioplasty site, followed by irradiating at that prior angioplasty site.

Moreover, it would not have been obvious to one of ordinary skill in the art to fully occlude a blood vessel using a fully inflated balloon catheter at a prior angioplasty site during laser irradiation, as the prior art teaches away from such a procedure. Previously cited Honye et al. teaches that the angioplasty-dilated site is subject to dissection, tearing and rupture (see Remarks, page 3, first complete paragraph). Further, U.S. Patent No. 5,766,584 to Edelman et al. (hereinafter "Edelman"), column 1, lines 44-51 discloses that when a balloon that is intravascularly inserted is overinflated, a variety of undesirable results occur, such as rupture of the tunica intima of the blood vessel. Therefore, one of ordinary skill in the art would not be motivated to use a completely inflated balloon and, in fact, would be taught away from using a completely inflated balloon during the PDT procedure in a post-angioplasty treatment. Therefore, contrary to the Examiner's assertion, it would not have been obvious to use a fully inflated balloon which fully occludes a blood vessel.

In complete contrast to the teachings of Honye and Edelman, in the present method, a portion or region of the blood vessel at the angioplasty-injured site is kept in tight contact with a completely inflated balloon which has been inserted within the vascular lumen, resulting in the lumen being distended. Further, the vascular lumen is distended when being irradiated using laser light during the PDT procedure, which results in obtaining the effect of increasing the cross-sectional area of the vascular lumen, as previously discussed on page 7, in the third complete paragraph, to page 8, first complete paragraph, of the Remarks section of the September 5, 2006



Amendment. Accordingly, the present procedure is completely unpredictable and non-obvious in view of the disclosure of Narciso.

With regard to Nyamekye, this reference teaches that when the PDT procedure, using the ALA-PPiX sensitizer, is applied at the same time as the angioplasty, the experimental intimal hyperplasia development, namely the restenosis in the blood vessel, can be inhibited in rats.

With regard to the newly cited reference of Antoshkiw, Antoshkiw discloses a conventional balloon catheter which has an inflated balloon, but is not equipped with an integrated optical fiber necessary for laser irradiation, and this conventional balloon catheter can never be utilized in the present invention, as claimed.

Based on the foregoing, Applicants respectfully submit that the present invention is not obvious in view of the cited prior art.

By this Amendment, Applicants have added new claims 7 and 8, which further recite that the laser fluence is at 664 nm wavelength and  $1 \text{ J/cm}^2$ , thus further distinguishing the present method over the prior art, which teaches 20 times the power at a different wavelength. Thus, the prior art discloses more than one order of magnitude more power than claims 7 and 8 recite. Applicants respectfully submit that the use of 1/20th the power, which is effective in the present method, represents an unexpected and surprising result over the prior art. Accordingly, claims 7 and 8 are not obvious in view of the prior art, which discloses irradiating at 20 times more power.

In view of the foregoing, Applicants respectfully submit that the present application is in condition for allowance.

**END REMARKS**